

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
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PCT

WRITTEN OPINION

(PCT Rule 66)

Date of Mailing (day/month/year) 01 OCT 2002	
Applicant's or agent's file reference CIT1410WO	REPLY DUE within 1 months/days from the above date of mailing
International application No. PCT/US01/24021	International filing date (day/month/year) 27 July 2001 (27.07.2001)
Priority date (day/month/year) 27 July 2000 (27.07.2000)	
International Patent Classification (IPC) or both national classification and IPC IPC(7): C07H 21/04; C12Q 1/68 and US Cl.: 435/6; 536/24.33	
Applicant CALIFORNIA INSTITUTE OF TECHNOLOGY	

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2 (a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application
3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension. See rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
 For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
 For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 27 November 2002 (27.11.2002).

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WRITTEN OPINION

International application No.

PCT/US01/24021

I. Basis of the opinion

1. With regard to the elements of the international application: *

- ☒ the international application as originally filed
- ☒ the description:
 - pages 1-41, as originally filed
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____
- ☒ the claims:
 - pages 42-47, as originally filed
 - pages NONE, as amended (together with any statement) under Article 19
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____
- ☒ the drawings:
 - pages 1-25, as originally filed
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____
- ☐ the sequence listing part of the description:
 - pages NONE, as originally filed
 - pages NONE, filed with the demand
 - pages NONE, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."

WRITTEN OPINION

International application No.
PCT/US01/24021

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO
Inventive Step (IS)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO
Industrial Applicability (IA)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO

2. CITATIONS AND EXPLANATIONS

Claims 1, 7, 9, 15, 20, 25, 28, 31-36, and 38 lack novelty under PCT Article 33(2) as being anticipated by Aoyagi et al. (US Patent 5,952,202). Aoyagi et al., disclose a method of conducting ligase chain reaction (LCR) where the formation of an amplification product is detected through the application of fluorescent resonance energy transfer (FRET). The aspect of using a two primers/ligators is considered to meet the limitation of a "first" and "second oligonucleotide." Also, the use of two fluorophores, wherein one donates energy so to excite the second, is considered to meet the limitation of a "selector tag" and a "detector tag," especially where as in claim 7 it is seen that the "selector tag" is a fluorescent moiety.

Claims 1, 7, 9, 15, 20, 25, 25, 31-36, and 38 lack an inventive step under PCT Article 33(3) as being obvious over Aoyagi et al. Aoyagi et al., disclose a method of conducting ligase chain reaction (LCR) where the formation of an amplification product is detected through the application of fluorescent resonance energy transfer (FRET). The aspect of using a two primers/ligators is considered to meet the limitation of a "first" and "second oligonucleotide." Also, the use of two fluorophores, wherein one donates energy so to excite the second, is considered to meet the limitation of a "selector tag" and a "detector tag," especially where as in claim 7 it is seen that the "selector tag" is a fluorescent moiety.

A review of Aoyagi et al., fails to find an explicit teaching of using a common or different selector tag, or different detector tags. While such teachings are not found, such would have been an obvious design choice on the part of a routineer in the art as the selector tag need only provide energy sufficient to energize the detector tag. A routineer in the art would have been motivated to have selected difference detector tags as such would allow for the independent detection of different amplification products, hereby readily expanding the usefulness of the assay.

Claims 2-6, 8, 10-14, 16-19, 21-24, 26, 27, 29-30, and 37 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed method of detecting nucleic acids, especially where a peptoid is used as a label on an oligonucleotide or where an oligonucleotide so labeled is combined in the kit.

----- NEW CITATIONS -----
US 6,952,202 A (AOYAGI et al.) 14 September 1999, see columns 4-8.

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International application No.
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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

TIME LIMIT:

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

V.1. Reasoned Statements:

The opinion as to Novelty was positive (Yes) with respect to claims 2-6, 8, 10-14, 16-19, 21-24, 26, 27, 29-30, and 37

The opinion as to Novelty was negative (No) with respect to claims 1, 7, 9, 15, 20, 25, 28, 31-36, and 38

The opinion as to Inventive Step was positive (Yes) with respect to claims 2-6, 8, 10-14, 16-19, 21-24, 26, 27, 29-30, and 37

The opinion as to Inventive Step was negative (NO) with respect to claims 1, 7, 9, 15, 20, 25, 28, 31-36, and 38

The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-38

The opinion as to Industrial Applicability was negative (NO) with respect to claims NONE